

Figure 1. Synthesis of MDMA-KLH Immunogen (10)

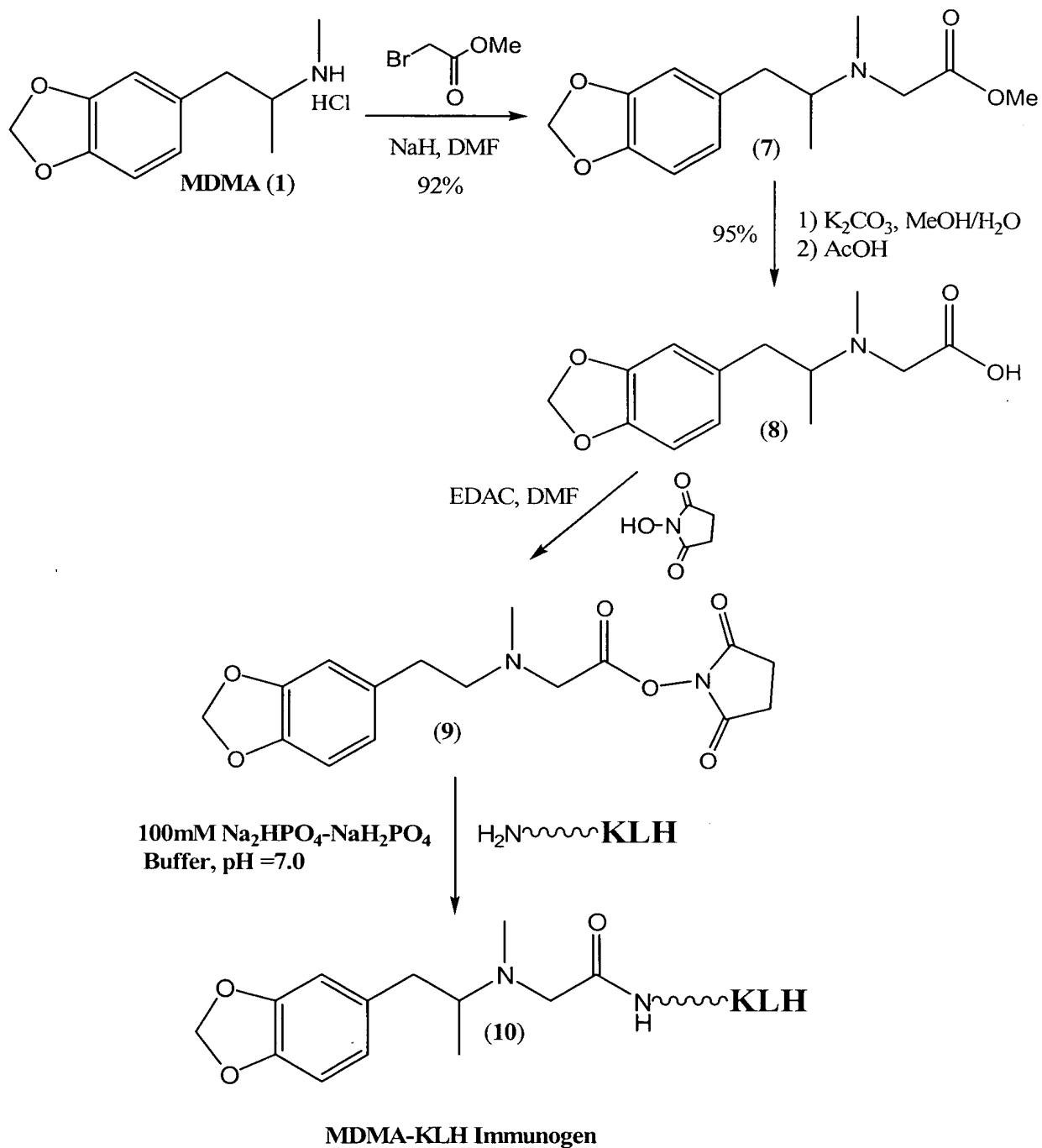


Figure 2. Synthesis of MDA-KLH Immunogen (14)

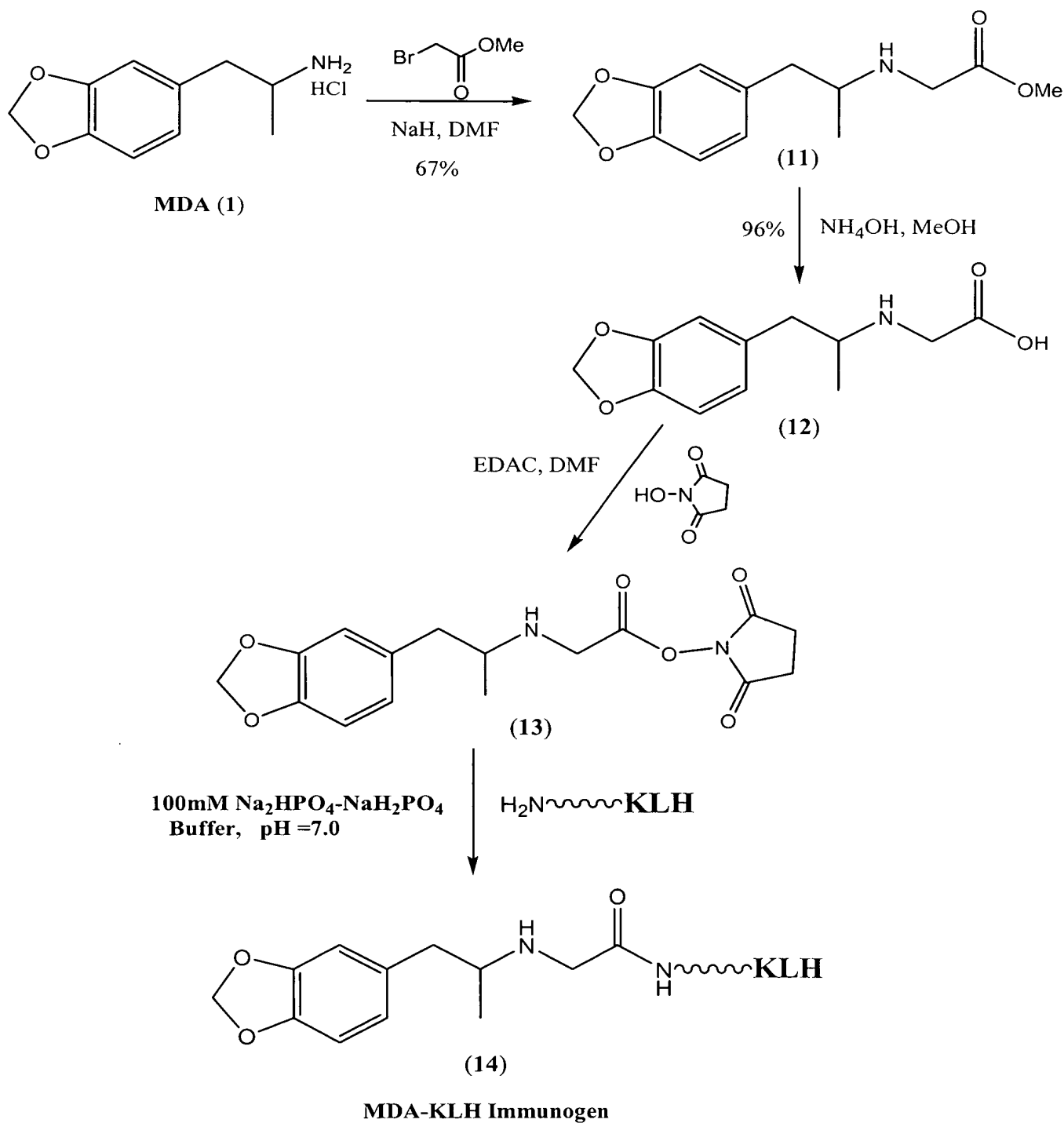


Figure 3. Synthesis of MDMA Haptens (15)-(17)

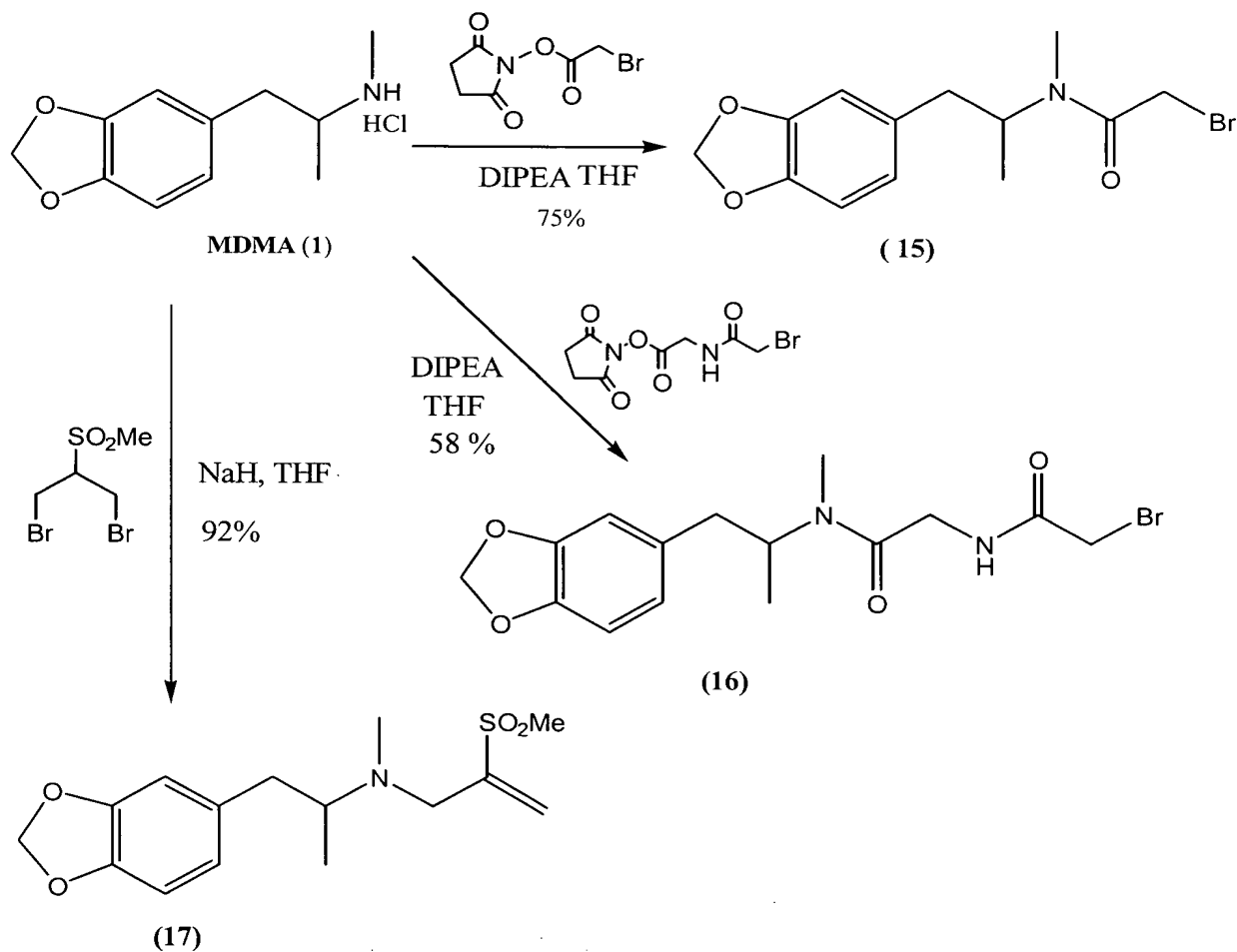


Figure 4A. Synthesis of MDA Haptens (18)-(19)

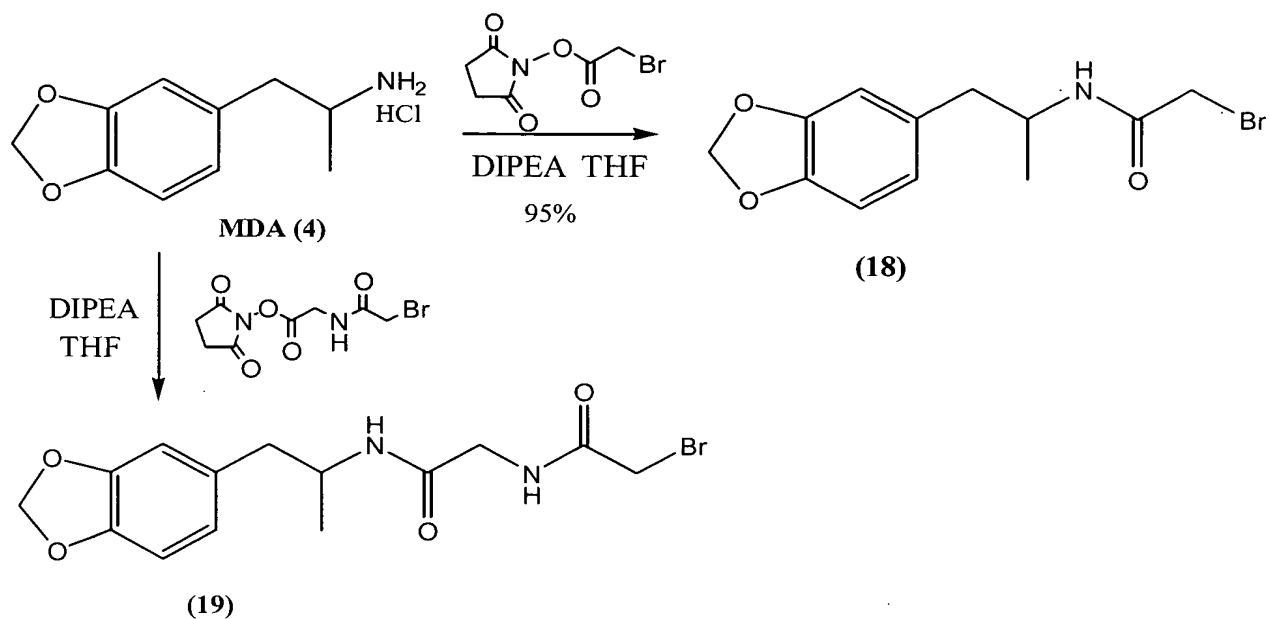


Figure 4B. Synthesis of MDA Hapten (20)

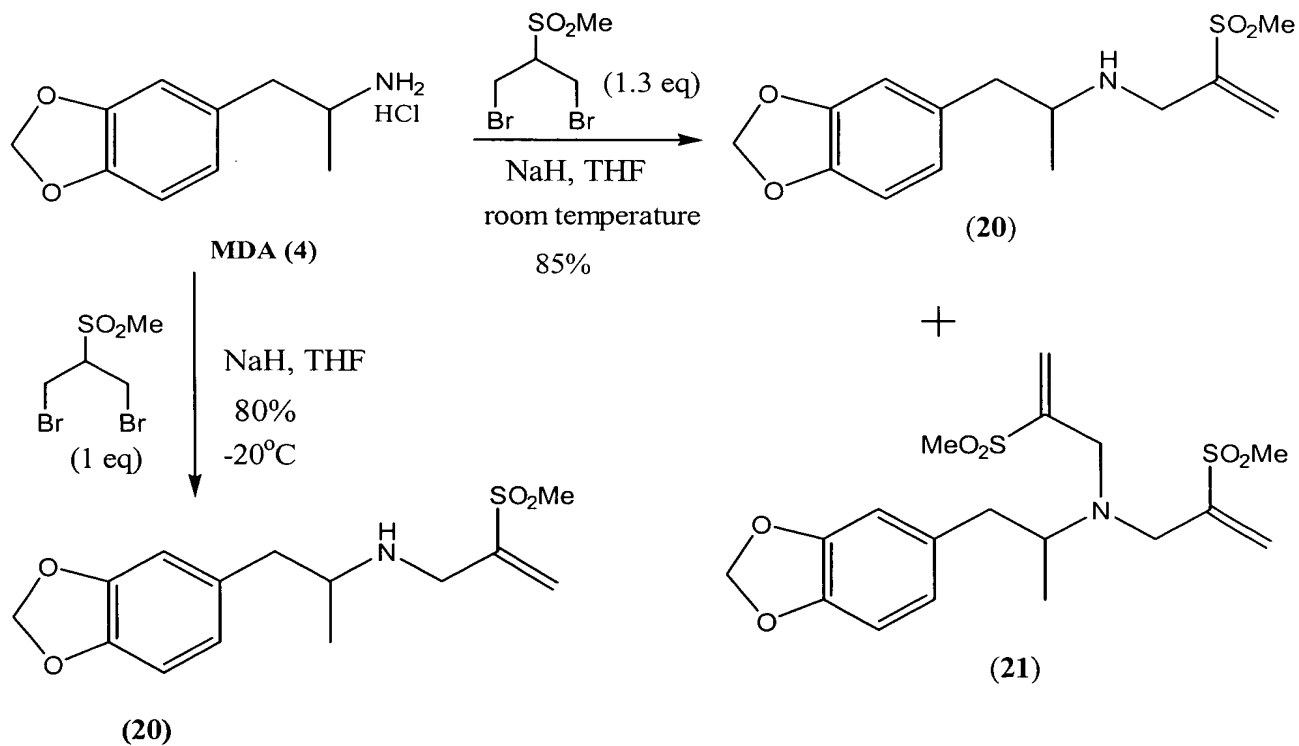


Figure 5. Synthesis of HMMA Intermediate (29) for Immunogen (30)

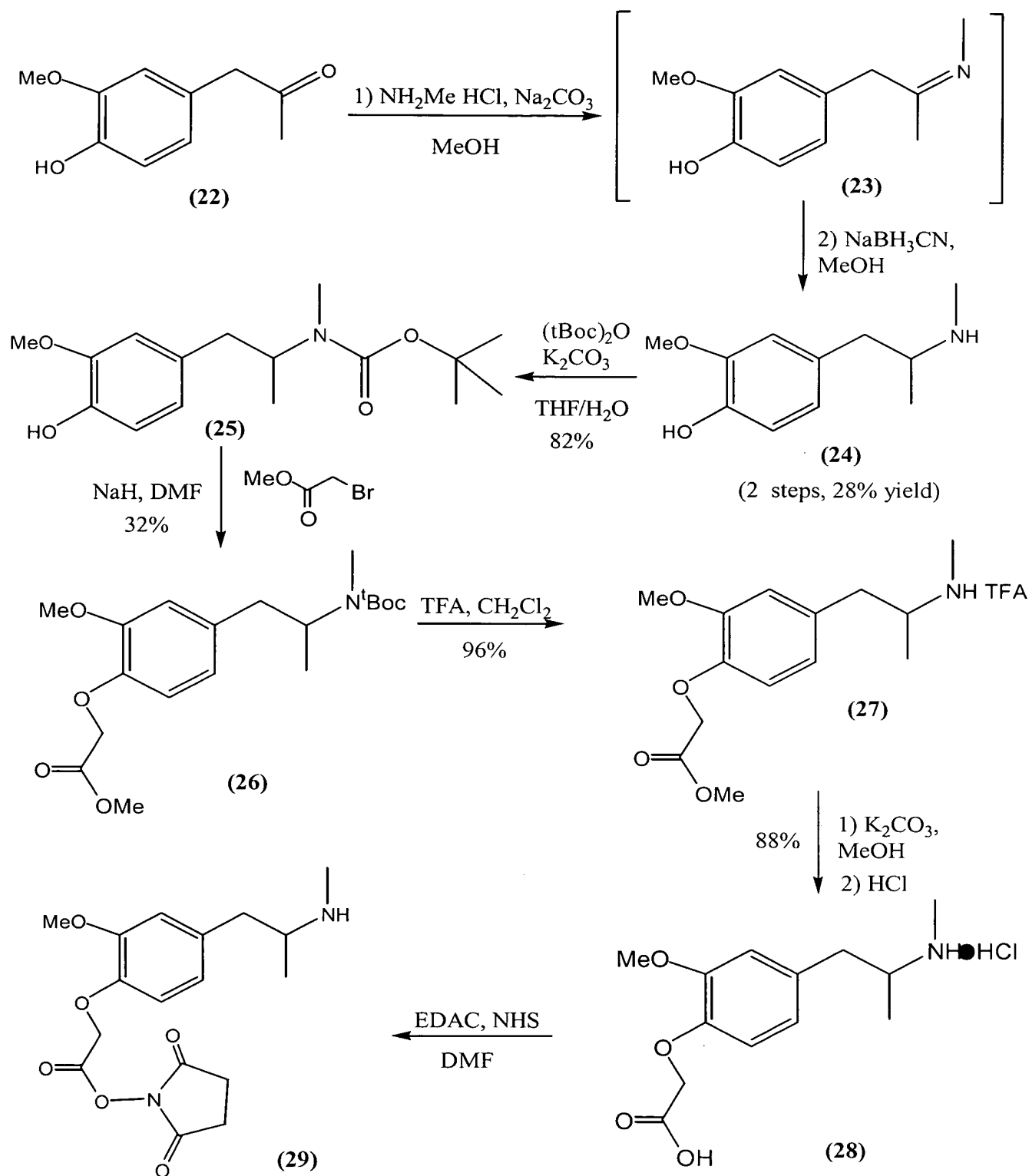
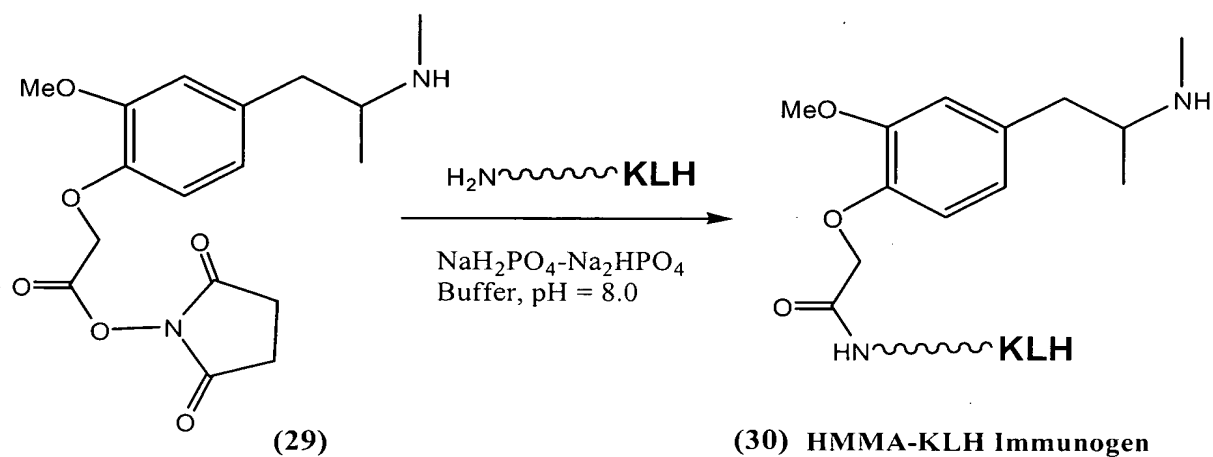


Figure 6. Synthesis of HMMA-KLH Immunogen (30)

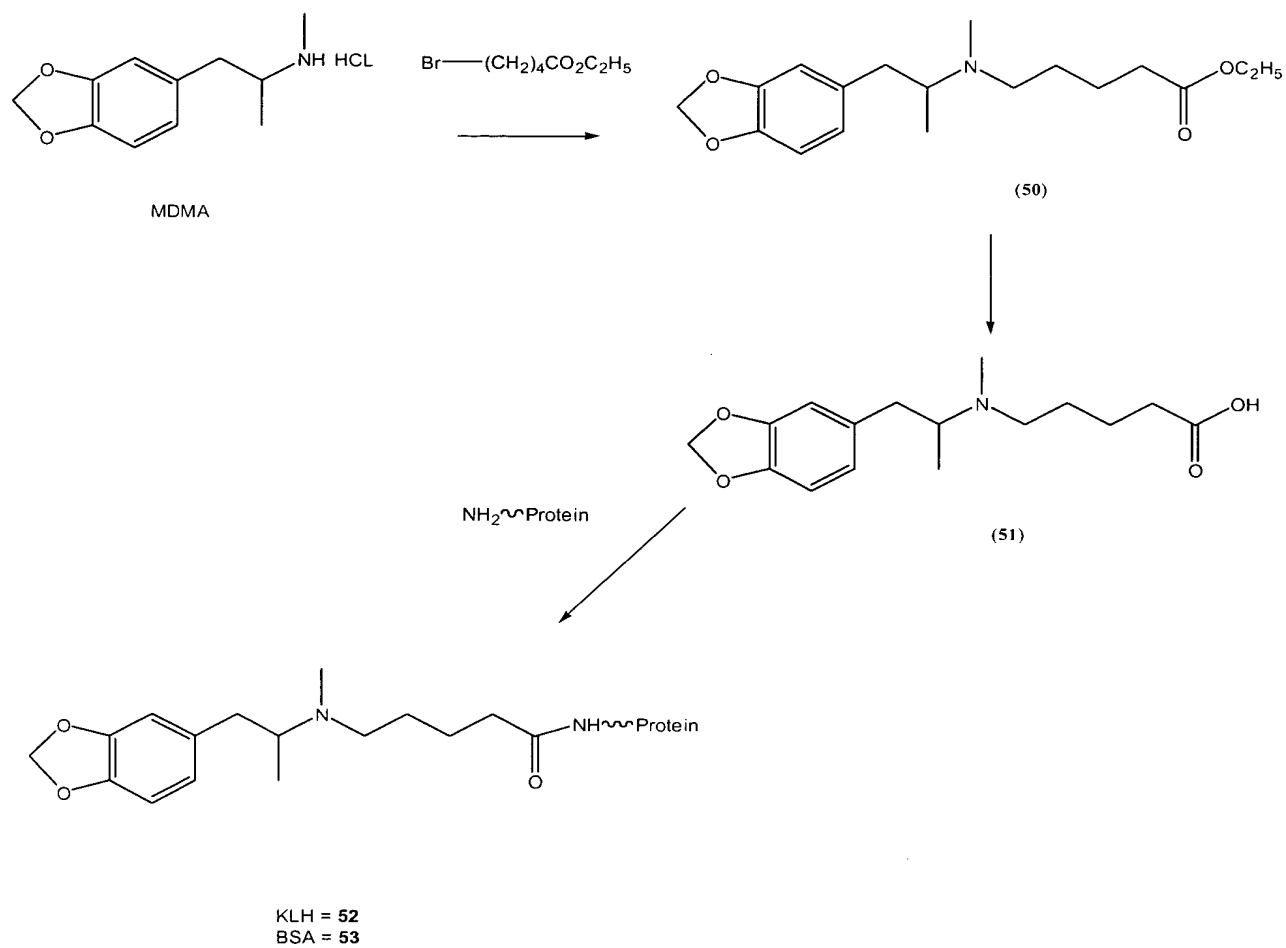


The synthesis of the HMMA-KLH immunogen (36) proceeds through several steps:

- Starting material (25):** 4-(4-methoxyphenyl)-2-methyl-1-(tert-butoxycarbonylamino)propane-1-ol derivative.
- Reaction 1:** Reaction with 1,2-dibromoethane ($\text{BrCH}_2\text{CH}_2\text{Br}$) in the presence of K_2CO_3 in Toluene yields intermediate **(31)** in 53% yield.
- Reaction 2:** Reaction of **(31)** with potassium acetate (KS-C(=O)CH_3) in $\text{MeOH}/\text{H}_2\text{O}$ yields intermediate **(32)** in 83% yield.
- Reaction 3:** Treatment of **(32)** with 1) TFA, CH_2Cl_2 followed by 2) K_2CO_3 , $\text{MeOH}/\text{H}_2\text{O}$ yields intermediate **(34)** in 83% yield.
- Reaction 4:** Reaction of **(34)** with the activated ester **(35)** (N-(2-bromoacetyl)-5-membered lactam) in a Buffer, pH = 8.0, yields the conjugate **(36)**.
- Alternative Path:** Direct reaction of **(34)** with KLH (keyhole limpet hemocyanin) yields the final immunogen **(36)**.

The final product **(36)** is the HMMA-KLH Immunogen, where the HMMA moiety is covalently linked to the KLH protein via a thioether bond.

FIG. 9



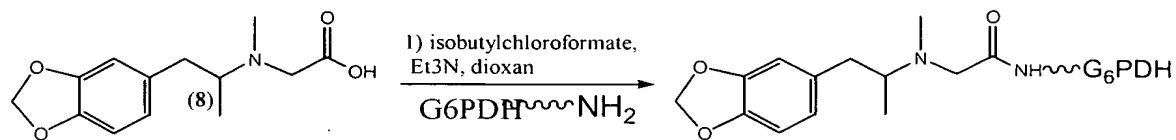


FIG. 10

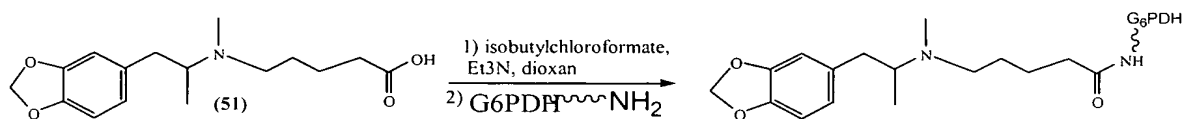


FIG. 11